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PATENT & TRADEMARK OFFICE

Attorney's Docket No. 1018793-000253

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of
Takeya Abe *et al.*

Application No.: 09/936,514

Filed: September 14, 2001

For: PROCESS FOR PURIFYING AMIDE COMPOUND

Group Art Unit: 1652

Examiner: Christian L. Fronda

Confirmation No.: 4410

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By: _____
Kim A. Cabello

APPEAL BRIEF

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Commissioner for Patents
P.O. Box 1450
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Sir:

This appeal is from the decision of the Primary Examiner dated May 2, 2007 finally rejecting claims 1, 3, 9, 11-16 and 25-31, which are reproduced as the Claims Appendix of this brief.

☐ A check covering the ☐ $ 250 ☐ $ 500 Government fee is filed herewith.

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The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

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I. Real Party in Interest

The present application is assigned to Mitsui Chemicals, Inc. and Mitsui Chemicals, Inc. is the real party in interest.

II. Related Appeals and Interferences

The Appellants' legal representative does not know of any other appeals or interferences which will affect or be directly affected by or have bearing on the Board's decision in the present appeal.

III. Status of Claims

Claims 1, 3, 9, 11-16 and 25-31 are pending in the application and have been rejected. Claims 2, 4-8, 10, 17-24 have been canceled. Claims 1, 3, 9, 11-16 and 25-31 are the subject of this appeal.

IV. Status of Amendments

An amendment was filed after final, but was not entered, in part because the recitation of a "pH of 3.5 to 6.5" allegedly raised new issues requiring an additional search. Appellants submit that this recitation was searched and present in claim 11 (pending and under examination since the time of filing of the present application). The claims last entered are set forth in the Claims Appendix, attached hereto.

V. Summary of Claimed Subject Matter

The invention relates to a process of purification of an amide compound using a combination of activated carbon, acidic conditions and hydratase. Claim 1 sets forth that the amide compound is purified by contacting an amide compound-containing solution with activated carbon under acidic conditions (see, *e.g.*, page 3, line 22-24) for removing a protein and separating activated carbon, wherein the amide compound has an unsaturated bond (see, *e.g.*, page 4, lines 7-8) and is produced by contacting a nitrile compound with a nitrile hydratase, a microorganism

fungus body containing nitrile hydratase or a processed product of the of the microorganism fungus body (see, *e.g.*, page 4, lines 9-13).

Dependent claims 3, 9, 11-16 and 25-31 are directed to the following subject matter and are supported in the specification as filed. Claims 3 and 25 set forth that the amide compound has from 2 to 20 atoms (see, *e.g.*, page 4, lines 5-6). Claim 9 sets forth that the amide compound is acrylamide or methacrylamide (see, *e.g.*, page 5, lines 2-3). Claims 11 and 26 set forth that the pH of the amide-containing solution is about 3.5-6.5 (see, *e.g.*, page 5, lines 6-9). Claims 12 and 27 set forth that the amide compound-containing solution is made acidic by use of an organic acid having an acid dissociation exponent of about 3.5 to 5.5 (see, *e.g.*, page 5, lines 10-13). Claims 13 and 28 recite that the organic acid is acrylic acid or methacrylic acid (see, *e.g.*, page 5, lines 15-17). Claims 14 and 29 recite that the process of purification uses an activated carbon from wood or palm shell as a raw material (see, *e.g.*, page 5, lines 18-20). Claims 15 and 30 recite that the temperature upon contact with said activated carbon is from 10 to 50°C (see, *e.g.*, page 5, lines 21-23). Claims 16 and 31 recite that the process is characterized in that after making said amide compound-containing solution in contact with said activated carbon, a liquid obtained by separating said activated carbon from said amide-containing solution is set at a saturation temperature or lower to deposit crystals (see, *e.g.*, bottom of page 5 to top of page 6).

VI. Grounds of Rejection to be Reviewed on Appeal

A. Rejection under 35 U.S.C. §112, first paragraph

Claims 1, 3, 9, 11-16 and 25-31 stand rejected under 35 U.S.C. §112, first paragraph, as purportedly failing to comply with the written description requirement. Final Office Action mailed May 2, 2007 at pages 2-3. In particular, the Office Action alleges that the claims do not recite amino acid sequences for nitrile hydratases.

B. Rejection under 35 U.S.C. §103

Claims 1, 3, 9, 11-16 and 25-31 stand rejected under 35 U.S.C. §103(a) as purportedly unpatentable over Oriel *et al.* (WO 99/55719) ("Oriel *et al.*") in view of Chen (*J Biol Chem.* 1967 Jan 25;242(2):173-81) ("Chen"). Final Office Action mailed

May 2, 2007, at pages 3-4. In particular, the Office Action alleges that one would be motivated to modify the teachings or Oriel *et al.* and combine the modified Oriel *et al.* reference with Chen.

VII. Argument

A. Rejection under 35 U.S.C. §112, first paragraph

In the rejection under 35 U.S.C. §112, first paragraph, the Examiner alleges that the claims fail to comply with the written description requirement. Final Office Action mailed May 2, 2007 at pages 2-3.

At page 2, part 3, paragraph 3, of the Office Action, the Examiner asserts that "recitation of the name 'nitrile hydratase' and its source as a microorganism fungus body do not define any structural features and amino acid sequences commonly possessed by the genus." The Examiner further asserts that the "specification does not describe and define any structural features and amino acid sequences commonly possessed by the genus."

The Examiner appears to take the position that, in order to satisfy the written description requirement of section 112, the specification is required to recite the amino acid sequence of every nitrile hydratase useful in the present method. In the absence of such extensive information, the Examiner suggests limiting the claimed method to a specific bacterial nitrile hydratase encoded by a specific polynucleotide sequence (see page 3, lines 8-11 of the pending office action).

The position of the Examiner is contrary to established case law. The purpose of the written description requirement was originally provided to prevent applicants from adding material to a claim that was not originally described in the specification. The written description requirement was developed to require disclosure of information that provides the inventive advances in the technology, *i.e.*, such that any new inventive information is added to the field of art. The written description requirement does not serve to require a treatise on what is well known in the art. As the courts have repeatedly indicated, a patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Spectra Physics, Inc. v. Coherent, Inc.*, 827

F.2d 1524, 3 USPQ2d 1737 (Fed. Cir. 1987); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

This holding has more recently been applied to nucleic acid and amino acid sequences. For example, the Federal Circuit has held, "None of the cases to which the Board attributes the requirement of total DNA re-analysis, *i.e.*, *Regents v. Lilly*, *Fiers v. Revel*, *Amgen*, or *Enzo Biochem*, require a re-description of what was already known." *Capon v. Eshhar v. Dudas*, 418 F.3d 1349, 1357 (Fed. Cir. 2005). The necessity of reciting sequence information for known proteins and genes was further addressed in *Falkner v. Inglis*, 79 USPQ2d 1001 (Fed. Cir. 2006). In *Falkner*, Falkner brought a motion challenging the Inglis application based upon written description for lacking description of any essential genes in poxvirus or describing the inactivation of such genes. In other words, Falkner challenged the specification for lacking written description of sequence information for genes in the poxvirus. The Federal Circuit, consistent with *Capon*, held:

> [A] requirement that patentees recite known DNA structures, ... would serve no goal of the written description requirement. It would neither enforce the *quid pro quo* between the patentee and the public by forcing the disclosure of new information, nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention.
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> ...
>
> Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly we hold that where, as in this case, accessible literature sources clearly provided ... their nucleotide sequences (here "essential genes")...

(*Falkner v. Inglis*, 79 USPQ2d at 1007-8).

The cases above side with Appellants position that the claimed invention is fully supported by the specification. Appellants have provided exemplary nitrile hydratases that can be used in the invention and one of skill in the art can readily identify a large number of other nitrile hydratases using routine skill and knowledge. Appellants submit that the combination of the instant disclosure coupled with the

knowledge of the skilled artisan sufficiently describes a genus of nitrile hydratases that may be used in the claimed method. As set forth in both *Capon* and *Falkner*, it is unnecessary to provide information that is already available to those of skill in the art. Furthermore, the recitation of a large number of nitrile hydratase sequences known in the art would serve no purposes under the written description requirement and would serve only to provide "unnecessary bulk to the specification." (*Falkner*, 79 USPQ2d at 1008).

Those of ordinary skill in the art were aware that nitrile hydratases are hydrolytic enzymes responsible for the sequential metabolism of nitriles in some bacteria and fungi and were capable of utilizing aliphatic nitriles as the sole source of nitrogen and carbon. Thus, those of ordinary skill in the art would have recognized from reading the disclosure that the inventors had invented a method that accommodates the use of various nitrile hydratases, not just the exemplary enzymes set forth in the specification. Neither the claims , nor the specification need be more specific with regard to, for example, the structure of a nitrile hydratases useful in the present methods because the skilled artisan already has such information in his/her possession.

As noted previously, the novelty of the present method lies not in the particular nitrile hydratase used in the method, but instead lies in the combination of conditions identified by the Appellants as suitable for purifying an amide compound. The forced recitation of a specific hydratase in the claims is an unnecessary limitation on the claimed method. Further, the forced recitation of known sequences in the instant disclosure would only add unnecessary bulk to the specification. Accordingly, accessible literature sources clearly provided, as of the relevant date, information about nitrile hydratase from various sources including those deposited in accessible repositories.

B. Rejection under 35 U.S.C. §103

Claims 1, 3, 9, 11-16 and 25-31 stand rejected under 35 U.S.C. §103(a) as purportedly unpatentable over Oriel *et al.* (WO 99/55719) ("Oriel *et al.*") in view of Chen. (*J Biol Chem.* 1967 Jan 25; 242(2):173-81) ("Chen"). Final Office Action

mailed May 2, 2007, at pages 3-4. The Examiner alleges that one of skill in the art would be motivated to modify the teachings of Oriel et al. to treat an amide compound at a more acidic pH, based upon Chen which allegedly teaches that acid pH is useful for lipid removal from proteins.

The Examiner must bear the initial burden to establish a *prima facie* case of obviousness before a rejection under 35 U.S.C. § 103 can be made or maintained. *See, In re Grabiak*, 769 F.2d 729, 733, 226 U.S.P.Q. 870, 873 (Fed. Cir. 1985). If a *prima facie* case is not established, then Appellants are entitled to a patent without presenting any further evidence of non-obviousness. *See, e.g. In re Oetiker*, 977 F.2d. 1443, 24 U.S.P.Q. 1443 (Fed. Cir. 1992)(citing *In re Grabiak*, *supra*).

To establish a *prima facie* case of obviousness, three criteria must be met: (1) All the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580, 583 (C.C.P.A. 1974). In this regard, all the words in a claim must be considered in judging the patentability of that claim against the prior art. *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970). (2) There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). (3) There must be a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 U.S.P.Q. 375 (Fed. Cir. 1986). The teaching or suggestion to make the claimed modification and the reasonable expectation of success must be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

The present claims are drawn to a method of purifying an amide compound by contacting a solution containing such a compound with activated carbon under acidic conditions (*i.e.*, pH 3.5 - 6.5) and a nitrile hydratase. Such conditions are conducive for removing protein contaminants. The amide compound includes an unsaturated bond and is produced by contacting a nitrile compound with a nitrile hydratase, a microorganism fungus body containing nitrile hydratase or a processed product of

the microorganism fungus body. Appellants were the first to discover that these conditions provide a purified compound with a high degree of reproducibility.

The Examiner alleges that the process taught by Oriel *et al.*, as modified by Chen, inherently removes impurities including, but not limited to, proteins. The Examiner further alleges that the modified process involves not only contacting the solution with activated carbon under acidic conditions (conditions which would result in instability of certain amide compounds), but also includes steps for concentrating or precipitating by distillation or evaporation the amide solution, thereby removing contaminating proteins. In arriving at the obviousness rejection, the Examiner has combined two distinct and divergent processes.

In contrast to the present claims, the methods disclosed by Oriel *et al.* are not conducive to removing contaminating proteins. This is because the contaminating proteins have a higher boiling point than that of the amide compound set forth in the claimed method. Accordingly, the contaminating proteins can not be distillated and evaporated at the lower temperature than the boiling point of the amide compound and the process of Oriel *et al.* can not inherently remove impurities including proteins. Further, Oriel *et al.* fails to teach or suggest that the proteins are included in the amide solution produced by contacting a nitrile compound with a nitrile hydratase, a microorganism fungus body containing nitrile hydratase or a processed product of the microorganism fungus body. Furthermore, Oriel *et al.* teach the use of neutral pH containing charcoal solution. As the data in the present application demonstrates, the inventors have unexpectedly and through thorough experimentation determined that acidic pH (not neutral pH) results in a better and more effective reproducible reaction.

It is clear from the specification of Oriel *et al.* that the cited reference fails to appreciate the significance of contacting the reaction solution with activated charcoal under acidic conditions in order to facilitate the purification of the amide compound as set forth in the pending claims. As noted in the present specification, utilizing charcoal treatment under the acidic conditions present in the amide solution provides an efficient and reproducible mechanism for removal of proteins. This treatment is

preferable to the charcoal treatment under "neutral conditions" taught in Oriel *et al.*. Thus, while the cited reference recites a purification mechanism, Oriel *et al.* clearly fails to disclose any method that utilizes acidic conditions of the reaction solution to facilitate the controlled purification of an amide compound. Accordingly, this reference supplies neither the motivation to use activated charcoal in conjunction with an acidic environment to arrive at a method as set forth in the pending claims, nor any expectation of success if one were to attempt it.

One of ordinary skill in the art attempting to overcome the deficiencies of the art (including Oriel *et al.*), would not be motivated to look to teachings of lipid and protein separation as taught by Chen, particularly if the interest of the research is directed to amide purification. Furthermore, one of skill in the art would not be motivated to use an acidic pH to purify amides. This is due to the well recognized polymerization and instability generated in acidic conditions of amides having unsaturated bonds. The only way to arrive at such a motivation is to use Appellants' disclosure as a template to piece together unrelated art reference and this is unquestionably not permitted.

The secondary reference of Chen is directed to protein-lipid separation. Chen does not remedy the deficiencies of Oriel *et al.* because Chen fails to suggest an acid charcoal treatment to remove proteins from a solution containing amide compounds. There is simply no motivation in either Oriel *et al.* or Chen to use acidic pH conditions, particularly pH 3.5 to 6.5, in order to generate a method suitable for purifying an amide compound under the acidic conditions set forth in the pending claims, and certainly no teaching that such experiments would have any likelihood of success. Chen, for example, teaches a pH of 3.0 and a temperature of an ice-bath (*i.e.*, ~0 °C) (see, *e.g.*, Chen at page 174, "Experimental Procedure"). Thus, Chen, the reference being used to modify Oriel et al., teach an ideal solution, *to remove lipids from proteins,* having a pH of 3.0 and being performed at 0 °C). This is in sharp contrast to Appellants' claimed invention which recites a pH range of 3.5 to 6.5 and a temperature of 10to 50 °C.

Appellants' independent claims are not taught or suggested by the combination of Oriel et al. and Chen. If an independent claim is non-obvious then any claim depending there from is also non-obvious.

Appellants submit that the each claim does not stand or fall together. Turning to the dependent claims, the Board will recognize that the combination of references do not teach or suggest each and every element of Appellants' dependent claims. For example, there is no teaching or suggestion in the references either alone or combined that teach a pH range of 3.5 to 6.5 as recited in claims 11 and 26. In fact, Chen, the reference being used to allegedly suggest this range, indicates at page 174, column 1, that the pH is 3.0 and the temperature is 0 °C. Furthermore, Appellants submit that the elements "acrylic acid" or "methacrylic acid" are not taught or suggest by either reference as set forth in claims13 and 28 or the dissociation exponents of 3.5-5.5 as set forth in claims 12 and 27. The Examiner's positions is that the selection of acids having such dissociation exponents as well as the selection of methacrylic acid are allegedly the subject of normal skill and thus do not require undue experimentation. Appellants respectfully disagree.

The elements of dependent claim 15-16 and 30-31 are not taught or suggested by the references either alone or in combination. For example, Chen specifically teaches that acid treatment of proteins and lipids is carried out in an ice-bath (*i.e.*, at 0 °C), in contrast, Appellants' claim that the temperature is about 10 to 50 °C.

From the foregoing, it is clear that the cited reference fails to support a *prima facie* case of obviousness. The cited prior art fails to teach or suggest every element of the claimed invention. Therefore, the reference can not render the invention obvious. In addition, Appellants have shown that the claimed method achieves unexpected results relative to the prior art methods. Accordingly, the rejection should be overturned and such action is earnestly requested.

VIII. Claims Appendix

See attached Claims Appendix for a copy of the claims involved in the appeal.

IX. Evidence Appendix

See attached Evidence Appendix for copies of evidence relied upon by Appellant.

X. Related Proceedings Appendix

No Related Proceedings Appendix is attached, because no related proceedings are identified in Section II, *supra*.

Respectfully submitted,

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Date January 17, 2008

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VIII. CLAIMS APPENDIX

The Appealed Claims

1. A purification process of an amide compound comprising contacting an amide compound-containing solution in contact with activated carbon under acidic conditions for removing a protein and separating activated carbon, wherein the amide compound has an unsaturated bond and is produced by contacting a nitrile compound with a nitrile hydratase, a microorganism fungus body containing nitrile hydratase or a processed product of the microorganism fungus body.

3. A purification process according to claim 2, wherein the amide compound has from 2 to 20 carbon atoms.

9. A purification process according to claim 3, wherein the amide compound is acrylamide or methacrylamide.

11. A purification process according to claim 9, wherein the amide compound-containing solution has pH of from 3.5 to 6.5 upon contacting with the activated carbon.

12. A purification process according to claim 11, characterized in that the amide compound-containing solution is prepared to be acidic by using an organic acid having an acid dissociation exponent of from 3.5 to 5.5 or by using said organic acid and a base.

13. A purification process according to claim 12, wherein the organic acid is acrylic acid or methacrylic acid.

14. A purification process according to claim 13, wherein the activated carbon is activated carbon made from wood or palm shell as a raw material.

15. A purification process according to claim 14, wherein a temperature upon contact with said activated carbon is from 10 to 50°C.

16. A purification process according to claim 15, characterized in that after making said amide compound-containing solution in contact with said activated carbon, a liquid obtained by separating said activated carbon from said amide-containing solution is set at a saturation temperature or lower to deposit crystals.

25. The purification process according to claim 1, wherein the amide compound has from 2 to 20 carbon atoms.

26. A purification process according to claim 10, wherein the amide compound-containing solution has pH of from 3.5 to 6.5 upon contacting with the activated carbon.

27. A purification process according to claim 26, characterized in that the amide compound-containing solution is prepared to be acidic by using an organic acid having an acid dissociation exponent of from 3.5 to 5.5 or by using said organic acid and a base.

28. A purification process according to claim 27, wherein the organic acid is acrylic acid or methacrylic acid.

29. A purification process according to claim 28, wherein the activated carbon is activated carbon made from wood or palm shell as a raw material.

30. A purification process according to claim 29, wherein a temperature upon contact with said activated carbon is from 10 to 50°C.

31. A purification process according to claim 30, characterized in that after making said amide compound-containing solution in contact with said activated carbon, a liquid obtained by separating said activated carbon from said amide-containing solution is set at a saturation temperature or lower to deposit crystals.

IX. EVIDENCE APPENDIX

None